## **Amendments to the Claims**

Claim 1 (original) A compound of Formula I:

$$R^{1}$$
 $N$ 
 $R^{2}$ 
 $R^{3}$ 

where:

 $R^1$  is  $(C_3-C_7$  cycloalkyl)<sub>0-1</sub> $(C_1-C_6$  alkyl),  $(C_3-C_7$  cycloalkyl)<sub>0-1</sub> $(C_2-C_6$  alkenyl),  $(C_3-C_7$  cycloalkyl)<sub>0-1</sub> $(C_2-C_6$  alkynyl) or  $C_3-C_7$  cycloalkyl, each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy,  $C_1-C_7$  alkoxy,  $C_3-C_7$  cycloalkoxy, oxo, and  $NR^4R^5$ , biphenyl optionally

substituted with halo, hydrogen,

 $R^2$  is  $C_1$ - $C_3$  alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl;

R<sup>3</sup> is:

i) a piperidin-2-yl moiety of formula:

ii) a tetrahydropyridin-2-yl moiety of formula:

iii) a piperazin-2-yl moiety of formula:

- iv) homopiperidin-2-yl;
- v) 1,2,3,4-tetrahydroisoquinolin-3-yl optionally substituted with one or two substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy;
- vi) 2-azabicyclo[2.2.2]oct-(5Z)ene-3-yl;
- vii) 2-azabicyclo[2.2.1]hept-3-yl optionally substituted with C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with C<sub>1</sub>-C<sub>4</sub> alkoxy; or
- viii) 2-azabicyclo[2.2.2]oct-3-yl optionally substituted with oxo, or optionally substituted with one or two substituents independently selected from hydroxy, fluoro, and C<sub>1</sub>-C<sub>6</sub> alkyl;

X is CH, N, or  $N^+-O^-$ ;

Y is CR<sup>11</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;

O is  $CR^{12}$ . N. or  $N^+$ -O<sup>-</sup>:

R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted up to three times with fluoro, or phenyl;

 $R^5$  is hydrogen,  $C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro, phenyl,  $-C(O)(C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro), or  $-SO_2(C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro);

R<sup>6</sup> and R<sup>7</sup> are independently selected from the group consisting of methyl, ethyl, and propyl;

R<sup>8</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>9</sup> is C<sub>3</sub>-C<sub>5</sub> cycloalkyl, <u>sec</u>-butyl, or -CH<sub>2</sub>R<sup>13</sup>;

 $R^{10}$  is  $-CF_2R^{14}$ ,  $-OR^{15}$ ,  $-CH_2C(O)CH_3$ ,  $-S(O)_{1-2}R^{16}$ ,  $-NR^{17}SO_2R^{18}$ ,  $(C_1-C_3$  alkoxy)-carbonyl, phenyl optionally substituted with halo, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxolan-2-yl, 1,3-dioxolan-2-yl, 1,1-dioxolan-2-yl, 1,3-dioxolan-2-yl, 1,1-dioxolan-2-yl, 1,1-dioxolan-2-yl, 1,3-dioxolan-2-yl, 1,1-dioxolan-2-yl, 1,3-dioxolan-2-yl, 1,1-dioxolan-2-yl, 1,1-dioxolan-2-y

dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1$ - $C_3$  alkyl;

 $R^{11}$  is hydrogen, chloro, isobutyl,  $CH_2R^{19}$ ;  $CF_2R^{20}$ , 1,1,1-trifluoro-2-hydroxyeth-2-yl,  $C_2$ - $C_4$  alkenyl optionally substituted with one or two fluorine atoms,  $OR^{21}$ ,  $C(O)R^{22}$ , N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl,  $N_1$ -dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithion-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

R<sup>12</sup> is hydrogen or fluoro;

R<sup>13</sup> is ethynyl or cyclopropyl;

R<sup>14</sup> is hydrogen or methyl;

R<sup>15</sup> is difluoromethyl or methanesulfonyl;

 $R^{16}$  is  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, phenyl, or  $-NR^{25}R^{26}$ ;

R<sup>17</sup> is hydrogen, C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with up to 3 fluorine atoms, or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

R<sup>18</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl or C<sub>3</sub>-C<sub>6</sub> cycloalkyl;

R<sup>19</sup> is fluoro, hydroxy, or C<sub>1</sub>-C<sub>3</sub> alkoxy;

R<sup>20</sup> is hydrogen, phenyl, or furyl;

 $R^{21}$  is  $C_1\text{-}C_3$  alkyl optionally substituted with one or two fluorine atoms;

 $R^{22}$  is  $C_1$ - $C_3$  alkyl,  $C_3$ - $C_5$  cycloalkyl,  $C_2$ - $C_3$  alkenyl,  $C_1$ - $C_3$  alkoxy,  $NR^{23}R^{24}$ , pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-

yl, phenyl, pyridinyl, or furyl;

R<sup>23</sup> is hydrogen or methyl;

R<sup>24</sup> is methyl, ethyl, or propyl;

R<sup>25</sup> is hydrogen or methyl;

R<sup>26</sup> is methyl; or

R<sup>25</sup> and R<sup>26</sup> taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

R<sup>29</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>30</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

 $R^{29}$  and  $R^{30}$  taken together with the carbon to which they are attached form a  $C_3$ - $C_6$  cycloalkyl ring;

 $R^{31}$  is hydrogen,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_6$  cycloalkyl, or phenyl optionally monosubstituted with  $C_1$ - $C_6$  alkyl;

 $R^{32}$  is hydrogen,  $R^{33}$ , or  $-(CH_2)_{0-2}$ -OR<sup>33</sup>;

 $R^{33}$  is  $C_1$ - $C_{10}$  alkyl optionally substituted with 1-6 fluorine atoms,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl, or - $(CH_2)_{0-3}$ - $R^{34}$ ;

 $R^{34}$  is  $C_3$ - $C_7$  cycloalkyl or phenyl each optionally substituted with one or two substitutents independently selected from the group consisting of halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, thienyl optionally substituted with halo, benzothienyl optionally substituted with halo, thiazolyl optionally substituted with  $C_1$ - $C_4$  alkyl, or adamantyl;

 $R^{35}$  is -(CH<sub>2</sub>)<sub>0-6</sub>- $R^{34}$ ,-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>- $R^{34}$ , -C(O)-(C<sub>1</sub>-C<sub>10</sub> alkyl), -C(O)-(C<sub>1</sub>-C<sub>4</sub> alkoxy optionally substituted with phenyl), C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1-6 fluorine atoms, C<sub>2</sub>-C<sub>10</sub> alkenyl, or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sup>36</sup> and R<sup>37</sup> are both hydrogen or, taken together with the carbon atom to which they are attached form a carbonyl group; or a pharmaceutically acceptable salt thereof; provided that: a) no more than one of X, Y, and Q may be N or N<sup>+</sup>-O<sup>-</sup>; and b) when X is CH, Y is CR<sup>11</sup>, and Q is CR<sup>12</sup>, then one of R<sup>11</sup> and R<sup>12</sup> is other than hydrogen.

Claims 2-5 (canceled)

Claim 6 (original): A pharmaceutical formulation comprising a compound of Claim 1, in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

Claim 7 (original): A compound of Formula III:

$$\begin{array}{c|cccc}
R^{27} & OR^{38} \\
\hline
R^1 & & & \\
O & R^2
\end{array}$$
III

where:

 $R^1$  is  $(C_3-C_7 \text{ cycloalkyl})_{0-1}(C_1-C_6 \text{ alkyl})$ ,  $(C_3-C_7 \text{ cycloalkyl})_{0-1}(C_2-C_6 \text{ alkenyl})$ ,  $(C_3-C_7 \text{ cycloalkyl})_{0-1}(C_2-C_6 \text{ alkynyl})$  or  $C_3-C_7 \text{ cycloalkyl}$ , each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl,

trifluoromethoxy, C<sub>1</sub>-C<sub>7</sub> alkoxy, C<sub>3</sub>-C<sub>7</sub> cycloalkoxy, oxo, and NR<sup>4</sup>R<sup>5</sup>, biphenyl optionally

substituted with halo, hydrogen,

 $R^2$  is  $C_1$ - $C_3$  alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl;

R<sup>3</sup> is:

ix) a piperidin-2-yl moiety of formula:

$$R^{28}$$
 $R^{29}$ 
 $R^{30}$ 
 $R^{31}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{32}$ 
 $R^{33}$ 

x) a tetrahydropyridin-2-yl moiety of formula:

$$R^{28}$$
 $R^{29}$ 
 $R^{30}$ 
 $R^{32}$ 
 $R^{32}$ 

xi) a piperazin-2-yl moiety of formula:

xii) homopiperidin-2-yl substituted in the 1-position with variable R<sup>28</sup>;

- xiii) 1,2,3,4-tetrahydroisoquinolin-3-yl substituted in the 1-position with variable R<sup>28</sup> and optionally further substituted with one or two substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy;
- xiv) 2-azabicyclo[2.2.2]oct-(5Z)ene-3-yl substituted in the 2-position with variable R<sup>28</sup>;
- xv) 2-azabicyclo[2.2.1]hept-3-yl substituted in the 2-position with variable  $R^{28}$  and optionally further substituted with  $C_1$ - $C_{10}$  alkyl optionally substituted with  $C_1$ - $C_4$  alkoxy; or
- xvi) 2-azabicyclo[2.2.2]oct-3-yl substituted in the 2-position with variable R<sup>28</sup> and optionally further substituted with oxo, or optionally further substituted with one or two substituents independently selected from hydroxy, fluoro, and C<sub>1</sub>-C<sub>6</sub> alkyl;

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X is CH, N, or N<sup>+</sup>-O<sup>-</sup>;
Y is CR<sup>11</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;
O is CR<sup>12</sup>, N, or N<sup>+</sup>-O<sup>-</sup>:
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R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted up to three times with fluoro, or phenyl;

 $R^5$  is hydrogen,  $C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro, phenyl,  $-C(O)(C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro), or  $-SO_2(C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro);

 $R^6$  and  $R^7$  are independently selected from the group consisting of methyl, ethyl, and propyl;

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R<sup>8</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;
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R<sup>9</sup> is C<sub>3</sub>-C<sub>5</sub> cycloalkyl, sec-butyl, or -CH<sub>2</sub>R<sup>13</sup>;

 $R^{10}$  is  $-CF_2R^{14}$ ,  $-OR^{15}$ ,  $-CH_2C(O)CH_3$ ,  $-S(O)_{1-2}R^{16}$ ,  $-NR^{17}SO_2R^{18}$ ,  $(C_1-C_3 \text{ alkoxy})$ -carbonyl, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1-C_3$  alkyl;

R<sup>11</sup> is hydrogen, chloro, isobutyl, CH<sub>2</sub>R<sup>19</sup>; CF<sub>2</sub>R<sup>20</sup>, 1,1,1-trifluoro-2-hydroxyeth-2-yl, C<sub>2</sub>-C<sub>4</sub> alkenyl optionally substituted with one or two fluorine atoms, OR<sup>21</sup>, C(O)R<sup>22</sup>, N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl, N,N-dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-

dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

R<sup>12</sup> is hydrogen or fluoro;

R<sup>13</sup> is ethynyl or cyclopropyl;

R<sup>14</sup> is hydrogen or methyl;

R<sup>15</sup> is difluoromethyl or methanesulfonyl;

R<sup>16</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, phenyl, or –NR<sup>25</sup>R<sup>26</sup>;

 $R^{17}$  is hydrogen,  $C_1$ - $C_3$  alkyl optionally substituted with up to 3 fluorine atoms, or  $C_3$ - $C_6$  cycloalkyl;

 $R^{18}$  is  $C_1$ - $C_3$  alkyl or  $C_3$ - $C_6$  cycloalkyl;

R<sup>19</sup> is fluoro, hydroxy, or C<sub>1</sub>-C<sub>3</sub> alkoxy;

R<sup>20</sup> is hydrogen, phenyl, or furyl;

R<sup>21</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with one or two fluorine atoms;

 $R^{22}$  is  $C_1$ - $C_3$  alkyl,  $C_3$ - $C_5$  cycloalkyl,  $C_2$ - $C_3$  alkenyl,  $C_1$ - $C_3$  alkoxy,  $NR^{23}R^{24}$ ,

pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

R<sup>23</sup> is hydrogen or methyl;

R<sup>24</sup> is methyl, ethyl, or propyl;

R<sup>25</sup> is hydrogen or methyl;

R<sup>26</sup> is methyl; or

 $R^{25}$  and  $R^{26}$  taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

R<sup>27</sup> is hydrogen or a nitrogen protecting group;

 $R^{28}$  is hydrogen or a nitrogen protecting group;

R<sup>29</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>30</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

 $R^{29}$  and  $R^{30}$  taken together with the nitrogen to which they are attached form a  $C_3$ - $C_6$  cycloalkyl ring;

 $R^{31}$  is hydrogen,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_6$  cycloalkyl, or phenyl optionally monosubstituted with  $C_1$ - $C_6$  alkyl;

 $R^{32}$  is hydrogen,  $R^{33}$ , or  $-(CH_2)_{0-2}$ -OR<sup>33</sup>;

 $R^{33}$  is  $C_1$ - $C_{10}$  alkyl optionally substituted with 1-6 fluorine atoms,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl, or -(CH<sub>2</sub>)<sub>0-3</sub>- $R^{34}$ ;

 $R^{34}$  is  $C_3$ - $C_7$  cycloalkyl or phenyl each optionally substituted with one or two substitutents independently selected from the group consisting of halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, thienyl optionally substituted with halo, benzothienyl optionally substituted with halo, thiazolyl optionally substituted with  $C_1$ - $C_4$  alkyl, or adamantyl;

 $R^{35}$  is -(CH<sub>2</sub>)<sub>0-6</sub>- $R^{34}$ ,-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>- $R^{34}$ , -C(O)-(C<sub>1</sub>-C<sub>10</sub> alkyl), -C(O)-(C<sub>1</sub>-C<sub>4</sub> alkoxy optionally substituted with phenyl), C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1-6 fluorine atoms, C<sub>2</sub>-C<sub>10</sub> alkenyl, or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sup>36</sup> and R<sup>37</sup> are both hydrogen or, taken together with the carbon atom to which they are attached form a carbonyl group;

 $R^{38}$  is hydrogen or an oxygen protecting group; or an acid addition salt thereof provided that: a) no more than one of X, Y, and Q may be N or  $N^+$ -O<sup>-</sup>; b) when X is CH, Y is  $CR^{11}$ , and Q is  $CR^{12}$ , then one of  $R^{11}$  and  $R^{12}$  is other than hydrogen; and c) at least one of  $R^{27}$ ,  $R^{28}$ , and  $R^{38}$  is other than hydrogen.

Claim 8 (original): A compound of Formula IV:

$$R^{39}$$
 $O$ 
 $R^{1}$ 
 $O$ 
 $R^{2}$ 
 $O$ 
 $R^{2}$ 

where:

 $R^1$  is  $(C_3-C_7 \text{ cycloalkyl})_{0-1}(C_1-C_6 \text{ alkyl})$ ,  $(C_3-C_7 \text{ cycloalkyl})_{0-1}(C_2-C_6 \text{ alkenyl})$ ,  $(C_3-C_7 \text{ cycloalkyl})_{0-1}(C_2-C_6 \text{ alkynyl})$  or  $C_3-C_7 \text{ cycloalkyl}$ , each optionally substituted with up to three groups independently selected from halo, hydroxy, thiol, cyano, trifluoromethyl, trifluoromethoxy,  $C_1-C_7$  alkoxy,  $C_3-C_7$  cycloalkoxy, oxo, and  $NR^4R^5$ , biphenyl optionally

substituted with halo, hydrogen,

 $R^2$  is  $C_1$ - $C_3$  alkyl, benzyl optionally monosubstituted in the phenyl ring with a substituent selected from the group consisting of halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, or benzyl optionally disubstituted in the phenyl ring with a first substituent independently selected from halo and a second substituent independently selected from halo,  $C_1$ - $C_6$  alkoxy optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl, and  $C_1$ - $C_6$  alkylthio optionally substituted in the alkyl chain with  $C_3$ - $C_7$  cycloalkyl;

R<sup>3'</sup> is:

ix) a piperidin-2-yl moiety of formula:

x) a tetrahydropyridin-2-yl moiety of formula:

$$R^{28}$$
  $R^{29}$   $R^{29}$   $R^{30}$   $R^{30}$   $R^{32}$   $R^{30}$   $R^{32}$   $R^{30}$   $R^{32}$   $R^{30}$ 

xii) a piperazin-2-yl moiety of formula:

- xii) homopiperidin-2-yl substituted in the 1-position with variable R<sup>28</sup>;
- xiii) 1,2,3,4-tetrahydroisoquinolin-3-yl substituted in the 1-position with variable R<sup>28</sup> and optionally further substituted with one or two substituents selected from halo, C<sub>1</sub>-C<sub>6</sub> alkyl, and C<sub>1</sub>-C<sub>6</sub> alkoxy;
- xiv) 2-azabicyclo[2.2.2]oct-(5Z)ene-3-yl substituted in the 2-position with variable R<sup>28</sup>;

- xv) 2-azabicyclo[2.2.1]hept-3-yl substituted in the 2-position with variable  $R^{28}$  and optionally further substituted with  $C_1$ - $C_{10}$  alkyl optionally substituted with  $C_1$ - $C_4$  alkoxy; or
- 2-azabicyclo[2.2.2]oct-3-yl substituted in the 2-position with variable R<sup>28</sup> and optionally further substituted with oxo, or optionally further substituted with one or two substituents independently selected from hydroxy, fluoro, and C<sub>1</sub>-C<sub>6</sub> alkyl;

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X is CH, N, or N<sup>+</sup>-O<sup>-</sup>;
Y is CR<sup>11</sup>, N, or N<sup>+</sup>-O<sup>-</sup>;
Q is CR<sup>12</sup>, N, or N<sup>+</sup>-O<sup>-</sup>:
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R<sup>4</sup> is hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl optionally substituted up to three times with fluoro, or phenyl;

 $R^5$  is hydrogen,  $C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro, phenyl,  $-C(O)(C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro), or  $-SO_2(C_1$ - $C_6$  alkyl optionally substituted up to three times with fluoro);

R<sup>6</sup> and R<sup>7</sup> are independently selected from the group consisting of methyl, ethyl, and propyl;

R<sup>8</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>9</sup> is C<sub>3</sub>-C<sub>5</sub> cycloalkyl, <u>sec</u>-butyl, or –CH<sub>2</sub>R<sup>13</sup>;

 $R^{10}$  is  $-CF_2R^{14}$ ,  $-OR^{15}$ ,  $-CH_2C(O)CH_3$ ,  $-S(O)_{1-2}R^{16}$ ,  $-NR^{17}SO_2R^{18}$ ,  $(C_1-C_3 \text{ alkoxy})$ -carbonyl, 1,3-dioxolan-2-yl, 1,3-dioxan-2-yl, 1,1-dioxo-2,3,4,5-tetrahydroisothiazol-2-yl, or tetrazol-5-yl optionally substituted with  $C_1-C_3$  alkyl;

 $R^{11}$  is hydrogen, chloro, isobutyl,  $CH_2R^{19}$ ;  $CF_2R^{20}$ , 1,1,1-trifluoro-2-hydroxyeth-2-yl,  $C_2$ - $C_4$  alkenyl optionally substituted with one or two fluorine atoms,  $OR^{21}$ ,  $C(O)R^{22}$ , N(methyl)(methylsulfonyl), N(methyl)(acetyl), pyrrolidin-2-on-1-yl, methylsulfonyl,  $N_1$ -dimethylaminosulfonyl, phenyl optionally substituted with one or two substituents selected from the group consisting of hydroxymethyl, methoxy, fluoro, and methylsulfonyl, 1,3-dioxolan-2-yl, 1,3-dithiolan-2-yl, 1,3-oxathiolan-2-yl, 1,3-dioxan-2-yl, 1,3-dithian-2-yl, pyridinyl, thiazolyl, oxazolyl, or 1,2,4-oxadiazolyl optionally substituted with methyl;

R<sup>12</sup> is hydrogen or fluoro;

R<sup>13</sup> is ethynyl or cyclopropyl;

R<sup>14</sup> is hydrogen or methyl;

R<sup>15</sup> is difluoromethyl or methanesulfonyl;

R<sup>16</sup> is C<sub>1</sub>-C<sub>4</sub> alkyl, C<sub>3</sub>-C<sub>6</sub> cycloalkyl, phenyl, or –NR<sup>25</sup>R<sup>26</sup>;

 $R^{17}$  is hydrogen,  $C_1$ - $C_3$  alkyl optionally substituted with up to 3 fluorine atoms, or  $C_3$ - $C_6$  cycloalkyl;

 $R^{18}$  is  $C_1$ - $C_3$  alkyl or  $C_3$ - $C_6$  cycloalkyl;

R<sup>19</sup> is fluoro, hydroxy, or C<sub>1</sub>-C<sub>3</sub> alkoxy;

R<sup>20</sup> is hydrogen, phenyl, or furyl;

R<sup>21</sup> is C<sub>1</sub>-C<sub>3</sub> alkyl optionally substituted with one or two fluorine atoms;

 $R^{22} \ is \ C_1\text{-}C_3 \ alkyl, \ C_3\text{-}C_5 \ cycloalkyl, \ C_2\text{-}C_3 \ alkenyl, \ C_1\text{-}C_3 \ alkoxy, \ NR^{23}R^{24},$ 

pyrrolidin-1-yl optionally substituted with methyl or one or two fluorine atoms, piperidin-1-yl, phenyl, pyridinyl, or furyl;

R<sup>23</sup> is hydrogen or methyl;

R<sup>24</sup> is methyl, ethyl, or propyl;

R<sup>25</sup> is hydrogen or methyl;

R<sup>26</sup> is methyl; or

R<sup>25</sup> and R<sup>26</sup> taken together with the nitrogen atom to which they are attached form a pyrrolidine or piperidine ring;

R<sup>28</sup> is hydrogen or a nitrogen protecting group;

R<sup>29</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>30</sup> is hydrogen or C<sub>1</sub>-C<sub>6</sub> alkyl;

R<sup>29</sup> and R<sup>30</sup> taken together with the nitrogen to which they are attached form a C<sub>3</sub>-C<sub>6</sub> cycloalkyl ring;

 $R^{31}$  is hydrogen,  $C_1$ - $C_6$  alkyl,  $C_3$ - $C_6$  cycloalkyl, or phenyl optionally monosubstituted with  $C_1$ - $C_6$  alkyl;

 $R^{32}$  is hydrogen,  $R^{33}$ , or  $-(CH_2)_{0-2}$ -OR<sup>33</sup>;

 $R^{33}$  is  $C_1$ - $C_{10}$  alkyl optionally substituted with 1-6 fluorine atoms,  $C_2$ - $C_6$  alkenyl,  $C_2$ - $C_6$  alkynyl, or -(CH<sub>2</sub>)<sub>0-3</sub>- $R^{34}$ ;

 $R^{34}$  is  $C_3$ - $C_7$  cycloalkyl or phenyl each optionally substituted with one or two substitutents independently selected from the group consisting of halo,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, hydroxy, trifluoromethyl, and trifluoromethoxy, thienyl optionally substituted with halo, benzothienyl optionally substituted with halo, thiazolyl optionally substituted with  $C_1$ - $C_4$  alkyl, or adamantyl;

 $R^{35}$  is -(CH<sub>2</sub>)<sub>0-6</sub>- $R^{34}$ ,-C(O)-(CH<sub>2</sub>)<sub>0-6</sub>- $R^{34}$ , -C(O)-(C<sub>1</sub>-C<sub>10</sub> alkyl), -C(O)-(C<sub>1</sub>-C<sub>4</sub> alkoxy optionally substituted with phenyl), C<sub>1</sub>-C<sub>10</sub> alkyl optionally substituted with 1-6 fluorine atoms, C<sub>2</sub>-C<sub>10</sub> alkenyl, or C<sub>2</sub>-C<sub>10</sub> alkynyl;

R<sup>36</sup> and R<sup>37</sup> are both hydrogen or, taken together with the carbon atom to which they are attached form a carbonyl group;

R<sup>38</sup> is hydrogen or an oxygen protecting group;

 $R^{39}$  and  $R^{40}$  are independently selected from methyl, ethyl, or propyl; or an acid addition salt thereof provided that no more than one of X, Y, and Q may be N or  $N^+$ -O<sup>-</sup>.

Claim 9 (new): A method for the inhibition of production of A- $\beta$  peptide comprising administering to a mammal in need of such treatment an effective amount of a compound of Claim 1.

Claim 10 (new): A method of inhibiting BACE in a mammal comprising administering to a mammal in need of such treatment an effective amount of a compound of Claim 1.